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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/225,233	01/04/99	CAMPBELL K	112800.401

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EXAMINER	
CROUCH, D	
ART UNIT	**PAPER NUMBER**
1632	6

DATE MAILED: 03/02/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/225,233	Campbell et al
Examiner	**Group Art Unit**
Deborah Crouch	1632

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three (3)* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-19* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-19* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☒ received in Application No. (Series Code/Serial Number) *08/802,282* .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3 & 4*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

This is a divisional of 08/802,282, allowed.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of copending Application No. 08/802,282, allowed. Although the conflicting claims are not identical, they are not patentably distinct from each other because the are of overlapping subject matter. Instant claims 1-10 are to methods of reconstituting an animal embryo by transferring the nucleus of a quiescent donor cell into a suitable recipient cell. Dependent claims define the animal as a cow, bull, pig, goat, sheep, camel or water buffalo, define the donor cell as being genetically modified, an embryonic, fetal or adult somatic cell; and define the recipient cell as an oocyte or an enucleated oocyte. Instant claims 11-13 are to methods for preparing an animal by reconstituting an animal embryo, causing the animal to develop to term and breeding from the animal. Dependent claims define the embryo as being manipulated prior to full development, and state that more than one animal is derived from the embryo. Instant claims 14-19 are to reconstituted animal embryos and animals made by transfer of a nucleus from a quiescent cell. Claims 1-2 of '282 are to methods of reconstituting a non-human mammalian embryo comprising transferring the nucleus of a quiescent diploid donor into a suitable enucleated recipient cell of the same species, activating the reconstituted cell and incubating the reconstituted cells so that an embryo develops. Dependent claims state that the recipient cell is an oocyte, that the mammal is a cattle, sheep, pigs, goats and camels, that the donor nucleus is genetically modified, that the donor cell is a differentiated, fetal or embryonic somatic cell. Claim 21 is to a

method of preparing a non-human mammal by transferring the reconstituted embryo to a female of the same species and developing the embryo into a non-human mammal. The instant claims are obvious over claims 1-21 of '282 because the instant specification defines "suitable recipient cell" as being enucleated or an enucleated oocyte, the donor cell as being a somatic adult cell or a differentiated somatic cell, and defines the method as including breeding the resulting animal. Thus it would have been obvious to the ordinary artisan at the time of the instant invention to take the instant claims to arrive at the invention of claims 1-21 or '282. The embryos and animals of instant claims 14-19 are obvious results of the methods of claims 1-21 in '282.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-19 are rejected under 35 U.S.C. 101 because they read on reconstituting a human embryo (1-13), a human reconstituted embryo (14-17) and a human (18-19). It is patent office policy not to allow claims to humans or claims that read on humans (1077 O.G. 24 April 21, 1987). Applicant can overcome this rejection by the insertion of the term "non-human" before animal.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of making a non-human mammalian embryo comprising transferring the nucleus of a donor cell of the same species as the embryo to an enucleated oocyte, wherein the donor cell has been incubated in media comprising 0.5% fetal calf serum to induce quiescence; and a method of

making a non-human mammal comprising transferring the nucleus of a donor cell of the same species as the mammal to an enucleated oocyte, wherein the donor cell has been incubated in media comprising 0.5% fetal calf serum to induce quiescence, does not reasonably provide enablement for methods of reconstituting all animal embryos or making all non-human animals, transferring the donor cell to a cell other than an enucleated oocyte of the same species and the donor cell being quiescent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification discloses only the production of animal embryos and non-human animals from quiescent cells or G0 cells (specification, page 8, lines 1-3), and not cells that are G1 arrested, which are not actively proliferating by means of the mitotic cell cycle. Thus there is no enablement for the use of G1 arrested cells as cell or nuclei donors as applicant did not contemplate such a use. Further the specification does not provided guidance for those methods that produce G1 arrested cells.

In the disclosure of using quiescent cells and nuclei from quiescent cells, the specification discloses only serum starvation as a means for inducing dividing cells into quiescence. There is no guidance or discussion of other means for causing cells to be quiescent, or how to obtain naturally quiescent cells. The need for quiescent cells is germane to the invention, and thus the specification should provide fully for all methods for producing quiescence, or sources, for quiescent cells.

As for recipient cells, the specification as well as the art teaches the use of enucleated oocytes as recipient cells. Oocytes are recognized as providing the proper environment to foster growth of a term animal from an embryo. It is unpredictable that any reprogramming could be effectively accomplished in cells other than oocytes. The specification does not teach other such cells. Further, enucleation, either physical or chemical, is required as the polyploidy which would result from using a non-enucleated embryo would prevent embryo development. Furthermore, there is no evidence that nuclear transfer to an oocyte or recipient cell of another species than the donor cell would provide the environment for a different species embryo to develop into a full term animal. Similarly, the specification does not provide guidance as to which embryonic stage development would occur.

With regards to the animal species produced by the claimed method the specification only provides guidance and direction for mammals. Other species, such as avian, have not been shown by the specification or the art the to be available for the manipulations required by the specification. Point in fact is that avian oocytes have not been shown to amenable to enucleation and transfer of a cell nucleus. At the time of filing, transgenic chickens were being made by administering the transgene via retroviral transduction of the early chicken embryo, and not by direct injection of a zygote as has been developed in mice (Brosselman et al., page 533, col. 1, parag. 1). Without access to chicken oocytes, the disclosed method will not be possible. Even in amphibians, the art does not provide guidance that the specification also does not with regard to the enucleation of oocytes . Further, as applicant's method of serum starvation to force cells into quiescence is the basis for chromatin remodeling or nuclear reprogramming, there is nothing the art or in the specification which would guide the artisan to successful remodel or reprogram avian or even amphibian cells. Without guidance from the specification, the skilled artisan would not have a reasonable expectation of success without an undue amount of experimentation to implement the claims for their breadth.

The specification does not teach the production of cross-species chimeric animals by the claimed method. Furthermore chimera production was regarded as unpredictable at the time of filing with regard to the percentage of one parent versus the other parent the chimera would have. In the production of sheep-goat chimeras, the chimeras had the appearance of lambs with some goat like wool (Fehilly et al. (1984) (page 635, col. 2, parag. 1). However, the reference also states that there was no prediction as to what percentage of the chimera was from the goat parent or how much was from the sheep parent. In addition, the art at the time of filing taught that in the production of chimeric goat-sheep, there were biases towards chimeras whose genotype and phenotype was most like that of the recipient, and that the successful production of chimeras resided in the neutralization of incompatibility between the chimeric embryo (Fehilly et al (1985), page 221, parag. 1). Thus the specification does not enable the claim as there is no enabled use for any chimeric, and the specification does not provide sufficient guidance to the production of an particular chimeric non-human animal. As for same species chimeric animals, the

specification provides no use for such animals. While they can be produced by the transfer of a blastomere as claimed, the use for such animals is not clear.

It is noted that the art as whole at the time of filing teaches that the donor cell, when cloning using non-embryonic, somatic or differentiated cells, some out-side event or external stimulus or condition needs to be applied to the cells for the nucleus to reprogram itself or re-model the genome such that it becomes totipotent. Fulka et al state that the success when embryonic cells were used as donor was likely due to the embryo cells not being completely differentiated at the time of transfer, and thus amenable to undergo full reprogramming (page 848, col. 1, parag. 1, line 1 to col. 2, line 1). Kono states that a break down of the nuclear envelop is necessary for reprogramming, as reprogramming probably requires the contact of the chromatin with the ooplasm (page 76, col. 2, parag. 2, lines 1-6). Wolf et al states that the coordination between cell cycles of donor and recipient cell is important to avoid DNA damage and to maintain correct ploidy of the embryo (Wolf, page 102, col. 2, lines 2-5). Wolf also states, and in support of Kono, that a donor nucleus is reprogrammed by the recipient cytoplasm, where the donor nucleus is reverted to the same morphological and temporal pattern of the zygote (Wolf, page 102, col. 1, lines 1-4). The only discernable method step that may permit the reprogramming of the cell and remodeling of the nucleus is the expansion of the donor cell in culture. As the reprogramming of the donor cell nucleus is important to the success of the method, applicant's have been given the scope rejection above.

The instant invention falls under the "germ of an idea" concept defined by the CAFC. The court has stated that "patent protection is granted in return for an enabling disclosure, not for vague intimations of general ideas that may or may be workable". The court continues to say that "tossing out the mere germ of an idea does not constitute an enabling disclosure" and that "the specification, not knowledge in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement". (See *Genetech inc v. Novo Nordisk A/S* 42 USPQ2d 1001, at 1005).

Thus at the time of filing, the skilled artisan would have needed to engage in an undue amount of experimentation to implement the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 contains an improper Markush grouping as male and female camels and water buffalo, respectively, are referred to as bulls and cows.

Claims 8-10 and 15-17 are unclear as at what age or stage of development would one determine an animal is an adult, fetus or embryo.

Claims 9 and 16 are additionally confusing as to the term "embryonic somatic cell". There are two types of cells: somatic and germ cells. As an embryo does not have germ cells, it does not have somatic cells. If applicant means by "somatic embryonic cells" all the cells of an embryo, then the claim is confusing as "somatic embryonic cells" implies other cell types in the embryo.

Claim 12 is vague as to the meets and bounds of "further manipulated". Exactly what does applicant include in such a term?

Claim 13 is confusing as to the term "derived". It would be clearer if applicant would use, as a suggestion, "made". The claim is also confusing as it does not reflect that which is disclosed. The specification discloses that more than one animal is made from an embryo when the embryo is disaggregated and the individual cells are used in NT procedures. Applicant is requested to clarify the claim.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14-19 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by US Patent 5,057,420 issued October 15, 1991 ('420).

The claims are drawn to reconstituted embryos and animals prepared by the claimed methods. However, a teaching of the same products obtained by a different method serves as anticipatory art against the instantly rejected claims.

'420 teaches bovine embryos and bovine offspring (col. 5-6, table 1). Claims 14-19 do not distinguish the embryos and animals claimed from the embryos and offspring taught by '420. Without a distinction which indicates a structural or functional difference between the claimed embryos and animals and those disclosed in '420, '420 clearly anticipates the claimed invention.

Claims 1-13 are free of the prior art. At the time of filing the prior art did not teach or suggest methods of reconstituting an animal embryo by transferring the nucleus of a quiescent cell into a recipient cell.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (703) 308-1126.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

The fax number is (703) 308-4242.

Please note the change in art unit number to Art Unit 1632. Please use this art unit number on all correspondence.

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630

Dr. D. Crouch
March 1, 2000